DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

December 9, 2014

EUROIMMUN US, INC.
C/O MR. MICHAEL LOCKE
DIRECTOR OF REGULATORY AFFAIRS
1100 THE AMERICAN ROAD
MORRIS PLAINS, NJ 07976

Re: k140224
Trade/Device Name: EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG)
Regulation Number: 21 CFR §866.5100
Regulation Name: Antinuclear Antibody Immunological Test System
Regulatory Class: Class II
Product Code: LKO, LKP, LLL, LJM, MQA
Dated: November 5, 2014
Received: November 6, 2014

Dear Mr. Locke:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Maria M. Chan -S

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and
Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k140224

Device Name
EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG) kit

Indications for Use *(Describe)*
The EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG) kit is an immune lineblot strip test intended for the qualitative detection of IgG class antibodies against nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1, CENP B and ribosomal P-proteins in human serum. Detection of these antibodies is used as an aid in the diagnosis of autoimmune diseases such as systemic lupus erythematosus, systemic sclerosis, poly-/dermatomyositis, mixed connective tissue disease and Sjögren's syndrome, in conjunction with other laboratory and clinical findings. The EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG) test kit is intended to be used in a clinical, reference or hospital laboratory. This kit is not designed for point-of-care testing.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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ATTACHMENT 1

510(k) SUBSTANTIAL EQUIVALENCE
SAFETY & EFFECTIVENESS SUMMARY

(*as required by 21 CFR § 807.92***)**

A. 510(k) Number:

K140224

B. Purpose for Submission:

New analyte(s)/new device [software previously cleared under EUROIMMUN EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) (K113439)]

C. Measurand:

Autoantibodies against nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1, CENP B, and ribosomal P-proteins

D. Type of Test:

Qualitative Immunoblot (Solid Phase ELISA)

E. Applicant:

EUROIMMUN US INC.

F. Proprietary and Established Names:

EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG)

G. Regulatory Information:

1. Regulation:
   21 CFR 866.5100- Antinuclear Antibody Immunological Test System
2. Classification:
   Class II
3. Product code:
   LJM
4. Panel:
   Immunology

H. Intended Use(s):

1. Intended Use(s):
   The EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG) kit is an immune lineblot strip test intended for the qualitative detection of IgG class antibodies against nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1, CENP B and ribosomal P-proteins in human serum. Detection of these antibodies is used as an aid in the diagnosis of autoimmune diseases such as systemic lupus erythematosus, systemic sclerosis, poly-/dermatomyositis, mixed connective tissue disease and Sjögren's syndrome, in conjunction with other laboratory and clinical findings. The EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG) test kit is intended to be used in a clinical, reference or hospital laboratory. This kit is not designed for point-of-care testing.
2. Indication(s) for Use:
   Same as Intended Use(s).
3. Special Conditions for Use Statement(s):

The EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG) test kit is intended to be used in a clinical, reference or hospital laboratory. This kit is not designed for point-of-care testing.
For Prescription Use Only.

4. Special Instrument Requirement(s):
   Not Applicable.

I. Device Description:

The EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG) consists of antigen coated test strips, a positive control, alkaline phosphatase-labelled anti-human IgG conjugate, sample buffer, wash buffer concentrate, NBT/BCIP substrate solution, incubation tray and test instruction. Evaluation protocol, reaction control card as well as further accessories for use with EUROLineScan are available separately.

J. Substantial Equivalence Information:

1. Predicate Device Name(s):
   EUROIMMUN and Inova Quanta Lite ELISAs (see table below).

2. Predicate 510(k) Number(s):

EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG) *Antigens*	**Predicate Device(s)**	**510(k) No.**
nRNP/Sm	EUROIMMUN Anti-nRNP/Sm ELISA (IgG)	k123261
Sm	EUROIMMUN Anti-Sm ELISA (IgG)	k123261
SS-A	EUROIMMUN Anti-SS-A ELISA (IgG)	k123261
Ro-52	Inova Quanta Lite™ SS-A 52 ELISA	k063565
SS-B	EUROIMMUN Anti-SS-B ELISA (IgG)	k123261
Scl-70	EUROIMMUN Anti-Scl-70 ELISA (IgG)	k123261
Jo-1	EUROIMMUN Anti-Jo-1 ELISA (IgG)	k123261
CENP B	EUROIMMUN Anti-Centromeres ELISA (IgG)	k123261
Ribosomal P-proteins	EUROIMMUN Anti-ribosomal P-proteins ELISA (IgG)	k123261

3. Comparison to Predicate Device(s):

Similarities

Item	**New device**		**Predicate device(s)**
Intended Use	Qualitative detection of IgG class antibodies against 8 different antigens: nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1, CENP B and rib. P-proteins in human specimens.		Same (when combined)
Reaction Principle	Enzyme immunoassay: enzyme labeled bound patient antibodies are detected with a chromogenic substrate that is converted to a visible colored product at the reaction site.		Same
Antigens	nRNP/Sm	Purified U1-nRNP complex; U1-nRNP contains RNP as well as Sm reactive proteins	Same
	Sm	Purified Sm antigen	Same
	SS-A	Purified SS-A antigen	Same
	Ro-52	Recombinant Ro-52 antigen	Same
	SS-B	Purified SS-B antigen	Same
	Scl-70	Purified Scl-70 antigen	Same
	Jo-1	Purified Jo-1 antigen	Same
	CENP B	Recombinant centromere protein B	Same
	Ribosomal P-proteins	Purified ribosomal P antigen	Same

Samples	Serum	Same

Differences

Item	New device	Predicate device(s)
Assay Format	Qualitative	Semi-Quantitative
Technology/ Procedure	Standard ELISA technique (solid phase ELISA): sample incubation with antigen coated strips, followed by a wash step, incubation with an anti-human IgG enzyme conjugate; wash step, incubation with substrate, wash step, air drying and evaluation.	Standard ELISA technique (solid phase ELISA): sample incubation with antigen coated wells, followed by a wash step, incubation with an anti-human IgG enzyme conjugate; wash step, incubation with substrate, stopping of the reaction with stop solution, photometric reading.
Sample Dilution	1:101 Dilution	EUROIMMUN: 1:201 dilution Inova: Serum, 1:101 dilution
Controls	Positive Control	EUROIMMUN: 2 controls (positive, negative) Inova: 3 controls (high positive, low positive, negative)
Conjugate	Alkaline phosphatase-labeled anti-human IgG	Anti-human IgG labeled with horseradish peroxidase
Substrate	BCIP/NBT	TMB
Reported Results	Positive/Negative (Qualitative)	EUROIMMUN: RU/ml or Ratios Inova: Units

K. Standard/Guidance Document Referenced (if applicable):

Guidance for Industry and FDA Staff: Recommendations for Anti-Nuclear Antibody (ANA) Test System Premarket (510(k)) Submissions (January 22, 2009)

Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline. CLSI document EP25-A. Wayne, PA: Clinical and Laboratory Standards Institute; September 2009.

L. Test Principle:

The procedure follows the EUROLINE technique that was cleared previously via the FDA 510(k) processes under 510(k) No. k113439. The assay can be evaluated visually or by means of the EUROLineScan software which was cleared under the k113439 process.

The EUROLINE uses different purified and recombinant antigens that have been coated and applied in easy to read lines onto a membrane. Antibodies are detected via a secondary antibody linked to an enzyme. The principle of the EUROLINE is that of an enzyme linked immunosorbent assay (ELISA), using a membrane as the solid phase instead of microtiter wells.

Patient samples are diluted 1:101 in sample buffer, 1.5 ml of diluted patient sample are added to the test strip lying in the incubation channel and incubated for 30 minutes at room temperature. After incubation the test strips are washed with wash buffer to remove unbound antibodies and 1.5 ml of the anti-human IgG enzyme conjugate reagent is added to each channel. After an additional 30-minutes incubation at room temperature, the test strips are again washed with wash buffer to remove any unbound enzyme conjugate and 1.5 ml of the substrate solution is added. The strips are incubated for 10 minutes at room temperature and then aspirated and washed with dist. water. The test strips can be evaluated visually by comparison of the band intensity with the reaction control card or they can be digitized by use of a flatbet scanner and evaluated with the computer software EUROLineScan.

The control band on the strips contains (non-specific) anti-human IgG, which reacts with the sample IgG to show a strong color reaction if the incubation was performed correctly and so represents a function test on each single strip. If the control band is negative, the test is invalid and should be repeated.

The positive control contains a mixture of the targeted antibodies which bind to the antigen coated on the blot strips. A strip incubated with the positive control shows a positive result. If the positive control is negative, the test results are invalid and should be repeated.

The qualitative results are reported for each individual antibody separately. The interpretation of the test results does not include a combined score or diagnosis.

M. Performance Characteristics (where applicable):

1. Analytical Performance:

   a. Precision/Reproducibility

   Reproducibility was investigated by repeated determinations of different samples covering the whole range of antigens of the EUROLINE ENA Profile 9 Ag (IgG).

   - Intra-Assay Reproducibility was investigated in 20 replicates on one day using the same kit lot.
   - Inter-Assay Reproducibility was investigated in 5 different runs, each run on a different day with 3 replicates per run, using the same kit lot.
   - Inter-Lot Reproducibility was tested in 6 different runs using different kit lots. Each run was performed in duplicates according to the package insert.
   - Inter-Observer Reproducibility was investigated by determinations of different samples covering the whole range of antigens of the EUROLINE ENA Profile 9 Ag (IgG). The samples were tested in 6 different runs. Each run was performed in duplicates according to the package insert and visually evaluated by two different technicians independently.

   Reproducibility was found to be sufficient as no positive sample was found negative and vice versa.

   b. Linearity/Assay Reportable Range:

   Not Applicable.

   c. Traceability, Stability, Expected Values (Controls, Calibrators or Methods):

   A recognized standard or reference material for antibodies against nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1, CENP B, dsDNA, nucleosomes, histones and ribosomal P-proteins is not available.

   Stability studies were conducted in accordance with the international standard DIN EN 13640:2002: Stability testing of in vitro diagnostics reagents (which was aligned by CLSI EP25-A). A real-time stability study was performed on original sealed and opened products to establish the shelf life claim and opened reagent stability claims. An accelerated stability study was performed for preliminary claims and transportation simulation at elevated temperatures. Another transportation simulation under freeze conditions was also performed. Three production lots of the EUROLINE ENA Profile 9 Ag (IgG) and an additional production lot for testing under “freeze” conditions were tested with three samples per antigen band. Acceptance criterium was that the results do not differ more than one result level from the reference run (real-time study: day 0; accelerated study and transportation simulation: 4°C stored sample). The studies support a minimum shelf life claim of 18 months for original sealed components and a stability claim of 12 months for opened components.

   d. Detection Limit:

   Not Applicable.

   e. Analytical Specificity:

   Cross-Reactivity: The reactivity of the EUROLINE ENA Profile 9 Ag (IgG) was verified using the CDC ANA reference panel. All samples were found in line with the CDC characterization.

   Interference: Different samples were spiked with potential interfering substances in 3 different concentrations. No interference was observed with hemolytic, lipemic or icteric samples for

concentrations of up to 500 mg/dl for haemoglobin, 2000 mg/dl for triglycerides and 40 mg/dl for bilirubin.

f. Assay Cut-off:

The cut-off intensity is defined as the lowest limit of a clearly visible band.

2. Analytical Performance:

a. Method Comparison

A comparison study was performed with clinically characterized samples obtained from different sources. The samples were tested with the EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG) and with the ELISA kits (k123261or k063565) as the predicate devices. For each parameter the same clinical disease groups were included as for the respective predicate ELISA. The results of the study are shown in the tables below. 95% C.I.'s were calculated by the exact method.

n = 936*		Predicate		Negative / Positive / Overall Agreement % (95% C.I.)
		positive	negative	
nRNP/Sm	**positive**	108	0	100.0% (99.2% - 100.0%)
	negative	14	814	88.5% (81.5% - 93.6%) 98.5% (97.5% - 99.2%)

*Patient samples: 225 SLE, 53 MCTD; Control samples: 211 SSc, 88 SS, 164 RA, 15 fibromyalgia, 22 gastrointestinal diseases, 10 liver diseases, 23 thyroid diseases, 10 muscle diseases, 11 skin diseases, 10 renal, 25 cancer, 69 infectious diseases
Sex: 133 men, 738 women, 65 unknown; Age: mean 50 y, range 2 to 91 y, 69 unknown

n = 917*		Predicate		Negative / Positive / Overall Agreement % (95% C.I.)
		positive	negative	
Sm	**positive**	29	2	99.8% (99.2% - 100.0%)
	negative	6	880	82.9% (66.4% - 93.4%) 99.1% (98.3% - 99.6%)

*Patient samples: 259 SLE; Control samples: 211 SSc, 88 SS, 164 RA, 15 fibromyalgia, 22 gastrointestinal diseases, 10 liver diseases, 23 thyroid diseases, 10 muscle diseases, 11 skin diseases, 10 renal, 25 cancer, 69 infectious diseases
Sex: 137 men, 715 women, 65 unknown; Age: mean 50 y, range 2 to 91 y, 69 unknown

n = 1036*		Predicate		Negative / Positive / Overall Agreement % (95% C.I.)
		positive	negative	
SS-A	**positive**	189	20	97.6% (96.4% - 98.6%)
	negative	1	826	99.5% (97.1% - 100.0%) 98.1% (97.0% - 98.8%)

*Patient samples: 229 SLE, 88 SS; Control samples: 211 SSc, 149 PM/DM, 164 RA, 15 fibromyalgia, 22 gastrointestinal diseases, 10 liver diseases, 23 thyroid diseases, 10 muscle diseases, 11 skin diseases, 10 renal, 25 cancer, 69 infectious diseases
Sex: 165 men, 806 women, 65 unknown; Age: mean 51 y, range 2 to 91 y, 69 unknown

n = 276*		Predicate		Negative / Positive / Overall Agreement % (95% C.I.)
		positive	negative	
Ro-52	**positive**	39	1	99.5% (97.5% - 100.0%)
	negative	18	218	68.4% (54.8% - 80.1%) 93.1% (89.5% - 95.8%)

*Patient samples: 81 SLE; Control samples: 15 fibromyalgia, 22 gastrointestinal diseases, 10 liver diseases, 23 thyroid diseases, 10 muscle diseases, 11 skin diseases, 10 renal, 25 cancer, 69 infectious diseases
Sex: 53 men, 158 women, 65 unknown; Age: mean 44 y, range 2 to 91 y, 69 unknown

n = 1036*		Predicate		Negative / Positive / Overall Agreement % (95% C.I.)
		positive	negative	
SS-B	**positive**	71	32	96.7% (95.4% - 97.7%)
	negative	0	933	100.0% (94.9% - 100.0%) 96.9% (95.7% - 97.9%)

*Patient samples: 229 SLE, 88 SS; Control samples: 211 SSc, 149 PM/DM, 164 RA, 15 fibromyalgia, 22 gastrointestinal diseases, 10 liver diseases, 23 thyroid diseases, 10 muscle diseases, 11 skin diseases, 10 renal, 25 cancer, 69 infectious diseases

Sex: 165 men, 806 women, 65 unknown; Age: mean 51 y, range 2 to 91 y, 69 unknown

n = 663*		Predicate		Negative / Positive / Overall Agreement % (95% C.I.)
		positive	negative	
Scl-70	**positive**	111	8	98.5% (97.1% - 99.4%)
	negative	4	540	96.5% (91.3% - 99.0%) 98. 2% (96.9% - 99.1%)

*Patient samples: 211 SSc; Control samples: 88 SS, 164 RA, 15 fibromyalgia, 22 gastrointestinal diseases, 10 liver diseases, 23 thyroid diseases, 10 muscle diseases, 11 skin diseases, 10 renal, 25 cancer, 69 infectious diseases, 5 artificial samples mixed to cut-off range
Sex: 111 men, 482 women, 70 unknown, 5 artificial; Age: mean 54 y, range 2 to 91 y, 74 unknown

n = 626*		Predicate		Negative / Positive / Overall Agreement % (95% C.I.)
		positive	negative	
Jo-1	**positive**	48	14	97.6% (96.0% - 98.7%)
	negative	0	564	100.0% (92.6% - 100.0%) 97.8% (96.3% - 98.8%)

*Patient samples: 169 PM/DM; Control samples: 88 SS, 164 RA, 15 fibromyalgia, 22 gastrointestinal diseases, 10 liver diseases, 23 thyroid diseases, 10 muscle diseases, 11 skin diseases, 10 renal, 25 cancer, 69 infectious diseases, 10 artificial samples mixed to cut-off range
Sex: 130 men, 421 women, 75 unknown; Age: mean 52 y, range 2 to 91 y, 79 unknown

n = 670*		Predicate		Negative / Positive / Overall Agreement % (95% C.I.)
		positive	negative	
CENP B	**positive**	51	5	99.2% (98.1% - 99.7%)
	negative	2	612	96.2% (87.0% - 99.5%) 99.0% (97.9% - 99.6%)

*Patient samples: 211 SSc; Control samples: 88 SS, 164 RA, 15 fibromyalgia, 22 gastrointestinal diseases, 10 liver diseases, 23 thyroid diseases, 10 muscle diseases, 11 skin diseases, 10 renal, 25 cancer, 69 infectious diseases, 12 artificial samples mixed to cut-off range
Sex: 111 men, 482 women, 77 unknown; Age: mean 54 y, range 2 to 91 y, 81 unknown

n = 615*		Predicate		Negative / Positive / Overall Agreement % (95% C.I.)
		positive	negative	
ribosomal P-proteins	**positive**	44	2	99.6% (98.7% - 100.0%)
	negative	8	561	84.6% (71.9% - 93.1%) 98.4% (97.0% - 99.2%)

*Patient samples: 273 SLE; Control samples: 55 SS, 90 RA, 15 fibromyalgia, 22 gastrointestinal diseases, 10 liver diseases, 23 thyroid diseases, 10 muscle diseases, 11 skin diseases, 10 renal, 25 cancer, 69 infectious diseases, 2 artificial samples mixed to cut-off range
Sex: 89 men, 434 women, 92 unknown; Age: mean 45 y, range 2 to 91 y, 97 unknown

b. Matrix Comparison:
Not Applicable.

3. Clinical Studies:

a. Sensitivity & Specificity:

Clinical studies were performed in cooperation with different sites (see below). In total 1279 clinically characterized samples were investigated for antibodies against nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1, CENP B and ribosomal P-proteins (IgG). The results obtained with the EUROIMMUN EUROLINE ENA Profile 9 Ag (IgG) are shown in the tables below. 95% C.I. are calculated by the exact method.

No.	Panel	n (men, women, unknown)	Mean age (age range, unknown)	EUROLINE ENA Profile 9 Ag (IgG) positive (%) (95% C.I.)								
				Anti-nRNP/ Sm	Anti-Sm	Anti-SS-A	Anti-Ro-52	Anti-SS-B	Anti-Scl-70	Anti-Jo-1	Anti-CENP B	Anti-rib. P-prot.
1	SLE	210 (14, 196)	41 y (16 – 80 y)	41 (19.5%) (14.4 – 25.5%)	18 (8.6%) (5.2 – 13.2%)	91 (43.3%) (36.5 – 50.3%)	74 (35.2%) (28.8 – 42.1%)	42 (20.0%) (14.8 – 26.1%)	0 (0.0%) (0.0 – 1.7%)	0 (0.0%) (0.0 – 1.7%)	3 (1.4%) (0.3 – 4.1%)	10 (4.8%) (2.3 – 8.6%)
2	SSc	211 (23, 188)	59 y (22 – 88 y)	3 (1.4%) (0.3 – 4.1%)	0 (0.0%) (0.0 – 1.7%)	22 (10.4%) (6.7 – 15.4%)	46 (21.8%) (16.4 – 28.0%)	10 (4.7%) (2.3 – 8.5%)	112 (53.1%) (46.1 – 60.0%)	2 (0.9%) (0.1 – 3.4%)	38 (18.0%) (13.1 – 23.9%)	0 (0.0%) (0.0 – 1.7%)
3a	Diffuse SSc	96							58 (60.4%) (49.9 – 70.3%)		6 (6.3%) (2.3 – 13.1%)	
3b	Limited SSc	113							6 (5.3%) (2.0 – 11.2%)		84 (74.3%) (65.3 – 82.1%)	
4	PM/DM	149 (38, 111)	56 y (14 – 85 y)	7 (4.7%) (1.9 – 9.4%)	1 (0.7%) (0.0 – 3.7%)	16 (10.7%) (6.3 – 16.9%)	67 (45.0%) (36.8 – 53.3%)	4 (2.7%) (0.7 – 6.7%)	1 (0.7%) (0.0 – 3.7%)	36 (24.2%) (17.5 – 31.8%)	4 (2.7%) (0.7 – 6.7%)	0 (0.0%) (0.0 – 2.4%)
5	MCTD	53 (7, 46)	44 y (20 – 69 y)	51 (96.2%) (87.0 – 99.5%)	3 (5.7%) (1.2 – 15.7%)	4 (7.5%) (2.1 – 18.2%)	10 (18.9%) (9.4 – 32.0%)	0 (0.0%) (0.0 – 6.7%)	0 (0.0%) (0.0 – 6.7%)	0 (0.0%) (0.0 – 6.7%)	1 (1.9%) (0.0 – 10.1%)	1 (1.9%) (0.0 – 10.1%)
6	Sjögren's	88 (4, 84)	52 y (19 – 78 y)	1 (1.1%) (0.0 – 6.2%)	1 (1.1%) (0.0 – 6.2%)	67 (76.1%) (65.9 – 84.6%)	68 (77.3%) (67.1 – 85.5%)	42 (47.7%) (37.0 – 58.6%)	0 (0.0%) (0.0 – 4.1%)	0 (0.0%) (0.0 – 4.1%)	3 (3.4%) (0.7 – 9.6%)	0 (0.0%) (0.0 – 4.1%)
7	RA	164 (43, 121)	54 y (19 – 80 y)	0 (0.0%) (0.0 – 2.2%)	0 (0.0%) (0.0 – 2.2%)	7 (4.3%) (1.7 – 8.6%)	9 (5.5%) (2.5 – 10.2%)	3 (1.8%) (0.4 – 5.3%)	1 (0.6%) (0.0 – 3.4%)	1 (0.6%) (0.0 – 3.4%)	2 (1.2%) (0.1 – 4.3%)	0 (0.0%) (0.0 – 2.2%)

No.	Panel	n (men, women, unknown)	Mean age (age range, unknown)	EUROLINE ENA Profile 9 Ag (IgG) positive (%) (95% C.I.)								
				Anti-nRNP/ Sm	**Anti-Sm**	**Anti-SS-A**	**Anti-Ro-52**	**Anti-SS-B**	**Anti-Scl-70**	**Anti-Jo-1**	**Anti-CENP B**	**Anti-rib. P-prot.**
8	Fibromyalgia	15 (0, 15)	58 y (42 – 76 y)	1 (6.7%) (0.2 – 31.9%)	0 (0.0%) (0.0 – 21.8%)	1 (6.7%) (0.2 – 31.9%)	1 (6.7%) (0.2 – 31.9%)	0 (0.0%) (0.0 – 21.8%)	0 (0.0%) (0.0 – 21.8%)	0 (0.0%) (0.0 – 21.8%)	1 (6.7%) (0.2 – 31.9%)	0 (0.0%) (0.0 – 21.8%)
9	Gastro-intestinal Diseases	22 (8, 7, 7)	36 y (2 – 74 y, 8)	0 (0.0%) (0.0 – 15.4%)	0 (0.0%) (0.0 – 15.4%)	0 (0.0%) (0.0 – 15.4%)	1 (4.5%) (0.1 – 22.8%)	0 (0.0%) (0.0 – 15.4%)	0 (0.0%) (0.0 – 15.4%)	0 (0.0%) (0.0 – 15.4%)	0 (0.0%) (0.0 – 15.4%)	0 (0.0%) (0.0 – 15.4%)
10	Liver Diseases	10		0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	4 (40.0%) (12.2 – 73.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)
11	Thyroid Diseases	23 (3, 20)	50 y (19 – 73 y)	0 (0.0%) (0.0 – 14.8%)	0 (0.0%) (0.0 – 14.8%)	0 (0.0%) (0.0 – 14.8%)	0 (0.0%) (0.0 – 14.8%)	0 (0.0%) (0.0 – 14.8%)	0 (0.0%) (0.0 – 14.8%)	0 (0.0%) (0.0 – 14.8%)	0 (0.0%) (0.0 – 14.8%)	0 (0.0%) (0.0 – 14.8%)
12	Muscle Diseases	10 (3, 6, 1)	62 y (31 – 91 y, 1)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)
13	Skin Diseases	11 (2, 7, 2)	61 y (40 – 84 y, 4)	0 (0.0%) (0.0 – 28.5%)	0 (0.0%) (0.0 – 28.5%)	0 (0.0%) (0.0 – 28.5%)	0 (0.0%) (0.0 – 28.5%)	0 (0.0%) (0.0 – 28.5%)	1 (9.1%) (0.2 – 41.3%)	0 (0.0%) (0.0 – 28.5%)	0 (0.0%) (0.0 – 28.5%)	0 (0.0%) (0.0 – 28.5%)
14	Renal Diseases	10 (5, 1, 4)	54 y (34 – 80 y, 4)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)	0 (0.0%) (0.0 – 30.8%)
15	Cancer	25		0 (0.0%) (0.0 – 13.7%)	0 (0.0%) (0.0 – 13.7%)	0 (0.0%) (0.0 – 13.7%)	1 (4.0%) (0.1 – 20.4%)	0 (0.0%) (0.0 – 13.7%)	0 (0.0%) (0.0 – 13.7%)	1 (4.0%) (0.1 – 20.4%)	0 (0.0%) (0.0 – 13.7%)	0 (0.0%) (0.0 – 13.7%)

No.	Panel	n (men, women, unknown)	Mean age (age range, unknown)	EUROLINE ENA Profile 9 Ag (IgG) positive (%) (95% C.I.)								
				Anti-nRNP/ Sm	Anti-Sm	Anti-SS-A	Anti-Ro-52	Anti-SS-B	Anti-Scl-70	Anti-Jo-1	Anti-CENP B	Anti-rib. P-prot.
16	Infectious Diseases	69 (20, 33, 16)	37 y (16 – 62 y, 17)	0 (0.0%) (0.0 –5.2%)	0 (0.0%) (0.0 – 5.2%)	1 (1.4%) (0.0 – 7.8%)	1 (1.4%) (0.0 – 7.8%)	0 (0.0%) (0.0 –5.2%)	0 (0.0%) (0.0 – 5.2%)	0 (0.0%) (0.0 – 5.2%)	0 (0.0%) (0.0 – 5.2%)	0 (0.0%) (0.0 – 5.2%)

b. Other Clinical Supportive Data (when a. and b. are not applicable):
Not Applicable.

4. Clinical Cut-off:
See Assay Cut-off.

5. Expected Values/Reference Range:

To establish the reference range of antibodies against nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1, CENP B and ribosomal P-proteins (IgG), 173 samples from US asymptomatic blood donors (79 men, 94 women, mean age 38.3 y, age range 19-50 y) were tested with the EUROLINE ENA Profile 9 Ag (IgG). The prevalence of the assay in the healthy group was 2.9%.

N. Performance Characteristics (where applicable):

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Performance Characteristics (where applicable):

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.

12.1.2014
Date

Michael Locke/Dir. Of Regulatory Affairs
Name/Title

Michael A. Locke
Signature